

REMARKS

I. THE AMENDMENTS

Claims 1-3, 8, and 10-11 were pending. Claims 1-3, 8, and 10-11 have been canceled, without prejudice to pursuing the canceled claims in this or other continuing applications. New claims 67-102 have been added. Upon entry of the present amendments, claims 67-102 will be pending and under active consideration. A marked version of the claims indicating the changes to the claims is attached hereto as Exhibit B. A copy of all the claims, as amended, is attached hereto as Exhibit C.

The specification has been amended to include the sequence identifiers in accordance with 37 C.F.R. §1.821 (c). A marked version of the specification indicating the changes to the specification is attached hereto as Exhibit A.

In particular, claims 1-3, 8, and 10-11 have been canceled and new claims 67-102 have been added to more particularly define what the Applicants regard as the invention. Support for the new claims can be found in the claims as originally filed and in the specification. In particular, support for Claims 67-99 can be found in the specification at page 9, line 35 through page 10, line 35, in Table 1, line 18, page 43, line 33 through page 44, line 35, in Example 11 beginning at page 131, and page 102, line 32 through page 104, line 26. Support for claims 100-102 can be found in the specification at page 6, lines 1-6, and in Example 11 beginning at page 131.

The amendments to the specification and claims do not constitute new matter as defined in 35 U.S.C. § 132. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

Applicant respectfully requests that the above-made amendments and remarks be entered and made of record in the file history of the instant application.

Respectfully submitted,

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39,445

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Enclosures

EXHIBIT A
MARKED VERSION OF THE SPECIFICATION AS AMENDED HEREIN
(Preliminary Amendment Filed February 19, 2002)
U.S. PATENT APPLICATION NO. 09/970,820

Page 11, lines 16 through 24:

4. DESCRIPTION OF THE FIGURES

FIG.1. In vivo cholesterol differential display. mRNA prepared from human monocytes isolated from the blood of patients on different diets. cDNA prepared from one patient on a high fat diet/high serum cholesterol (lanes 1,2) and low fat diet/low serum cholesterol (lanes 3,4) was displayed using the forward primer T₁₁XG (SEQ ID NO. 8) and the reverse primer OPO14 (agcatggctc)(SEQ ID NO. 9). The DNA corresponding to marked band (#14) was excised and amplified for sequence analysis.

Page 11, line 31 through page 12, line 28:

FIG.3. Quantitative RT-PCR analysis of mouse bcl-2 mRNA levels in apoE-deficient mice. Monocyte RNA from apoE-deficient and control mice was compared using primers for mouse bcl-2 [(for-caccctggcatcttctcctcc/rev-atcctccccagttcaccccatcc)] (for-caccctggcatcttctcctcc (SEQ ID NO. 10) /rev-atcctccccagttcaccccatcc (SEQ ID NO. 11)) shown in the upper panel and mouse γ Actin [(for-cctgatatagggcactgtgt/rev-gaacacggcattgtcactaact)] (for-cctgatatagggcactgtgt (SEQ ID NO. 12)/rev-gaacacggcattgtcactaact (SEQ ID NO. 13)) shown in the lower panel. A 1:3 dilution series of each input cDNA was done in pairs with the left band in each pair deriving from wild-type cDNA and the right band from apoE-deficient cDNA.

FIG.4. RT-PCR quantification of human glutathione peroxidase (HUMGPXP1) cDNA from human clinical samples cDNA prepared from RNA derived from blood

monocytes of the same patient under a high fat diet (serum cholesterol level = 200; top panel) and a low fat diet (serum cholesterol level = 170; bottom panel). Dilution series of amplification products using GPX1.3 primers derived from HUMGPXP1 sequences 1121-1142 (for-aagtcgcgccccccctgaaat) (SEQ ID NO. 14) and 1260-1237 (rev-gatccctggccaccgtccgtctga)(SEQ ID NO. 15) is shown in the left portion of each panel. Dilution series of amplification products using human actin primers [(for-accctgaagtacccat/rev-tagaagcatttgcggtg)] (for-accctgaagtaccccat (SEQ ID NO. 16)/rev-tagaagcatttgcggtg (SEQ ID NO. 17)) is shown in the right portion of each panel. The HUMGPXP1 band decreased in intensity under a high fat diet (compare top left to bottom left), whereas the actin control band was equally intense under each diet (compare top right to bottom right).

FIG.5. IL-1 activated HUVEC differential display. mRNA prepared from control HUVEC (lanes 9,10), 1 hr. of 10 units/ml IL-1 treatment (lanes 7,8), or 6 hr. treatment (lanes 11,12), was used in differential display reactions with the forward primer OPE7 (agatgcagcc) (SEQ ID NO. 18) and reverse primer T₁₁XA (SEQ ID NO. 19), which is an equimolar mix of oligonucleotides where X is G, C, or A. The DNA corresponding to marked band, rchd005, was excised and amplified for Northern analysis and subcloning.

Page 13, lines 1 through 13:

FIG.8. Band rchd005 DNA sequence (SEQ ID NO. 1). The sequence was determined by sequencing the insert of pRCHD005, resulting from the ligation of amplified rchd005 sequences into the TA cloning vector.

FIG.9. IL-1 activated HUVEC differential display. mRNA prepared from control HUVEC (lanes 3,4), 1 hr. of 10 units/ml IL-1 treatment (lanes 1,2), or 6 hr. treatment (lanes

5.6), was used in differential display reactions with the forward primer OPG20 (tctccctcag)(SEQ ID NO. 20) and reverse primer T₁₁XC (SEQ ID NO. 21), which is an equimolar mix of oligonucleotides where X is G, C, or A. The DNA corresponding to marked band, rchd024, was excised and amplified for Northern analysis and subcloning.

Page 13, line 25 through page 14, line 23:

FIG.12. Band rchd024 DNA sequence (SEQ ID NO. 2). The sequence was determined by sequencing the insert of pRCHD024, resulting from the ligation of amplified rchd024 sequences into the TA cloning vector.

FIG.13. IL-1 activated HUVEC differential display for rchd032. mRNA prepared from control HUVEC (lanes 3,4), 1 hr. of 10 units/ml IL-1 treatment (lanes 1,2) , or 6 hr. treatment (lanes 5,6), was used in differential display reactions with the forward primer OPI9 (tggagagcag)(SEQ ID NO. 22) and reverse primer T₁₁XA, which is an equimolar mix of oligonucleotides where X is G, C, or A. The DNA corresponding to marked band, rchd032, was excised and amplified for Northern analysis and subcloning.

FIG.14. RT-PCR quantification of rchd032 cDNA from IL-1 activated HUVEC's cDNA prepared from RNA derived from control, 1hr., and 6 hr. IL-1 activated HUVEC's. Shown in lanes 1,2, and 3 are a 5 fold dilution series of input cDNA amplified in the upper panel with rchd032 primers [(for-atttataaaggggtaattcatta/rev-ttaaagccaatttcaaaataat)] (for-atttataaaggggtaattcatta)(SEQ ID NO. 23)/rev-ttaaagccaatttcaaaataat)(SEQ ID NO. 24)), and in the lower panel with human actin primers (for-accctgaagtaccccat/rev-tagagcatttgcggtg). A band at the 1:125 dilution in lane 3 is visible in the 6 hr. sample but not in the control.

FIG.15. Band rchd032 DNA sequence (SEQ ID NO. 3). The sequence was determined by sequencing the insert of pRCHD032, resulting from the ligation of amplified

rchd032 sequences into the TA cloning vector.

FIG.16. IL-1 activated HUVEC differential display for rchd036. mRNA prepared from control HUVEC (lanes 3,4), 1 hr. of 10 units/ml IL-1 treatment (lanes 1,2), or 6 hr. treatment (lanes 5,6), was used in differential display reactions with the forward primer OPI17 (ggtggtgatg)(SEQ ID NO. 25) and reverse primer T₁₁XC, which is an equimolar mix of oligonucleotides where X is G, C, or A. The DNA corresponding to marked band, rchd036, was excised and amplified for Northern analysis and subcloning.

Page 14, lines 31 through 34:

FIG.18. Band rchd036 DNA sequence (SEQ ID NO. 4). The sequence was determined by sequencing the insert of pRCHD036, resulting from the ligation of amplified rchd036 sequences into the TA cloning vector.

Page 15, lines 20 through 32:

FIG.22. Band rchd502 DNA sequence (SEQ ID NO. 5). The sequence was determined by sequencing the insert of pRCHD502, resulting from the ligation of amplified rchd502 sequences into the TA cloning vector.

FIG.23. Laminar shear stress HUVEC differential display for rchd505. mRNA prepared from control HUVEC (lanes 3,4), 1 hr. (lanes 1,2) or 6 hr. (lanes 5,6) of 10 dyn/cm² laminar shear stress treatment was used in differential display reactions with the forward primer OPE2 (ggtgcgggaa) (SEQ ID NO. 26) and reverse primer T₁₁XA, which is an equimolar mix of oligonucleotides where X is G,C, or A. The DNA corresponding to marked band, rchd505, was excised and amplified for Northern analysis and subcloning.

Page 16, line 9 through Page 17, line 2:

FIG.26. Laminar shear stress HUVEC differential display for rchd523. mRNA prepared from control HUVEC (lanes 3,4), 1 hr. (lanes 1,2) or 6 hr. (lanes 5,6) of 10 dyn/cm² laminar shear stress treatment was used in differential display reactions with the forward primer OPI11 (acatgccgtg) (SEQ ID NO. 27) and reverse primer T₁₁XC, which is an equimolar mix of oligonucleotides where X is G,C, or A. The DNA corresponding to marked band, rchd523, was excised and amplified for Northern analysis and subcloning.

FIG.27. RT-PCR quantification of rchd523 cDNA from shear stressed endothelial cell cDNA prepared from RNA derived from control, 1hr., and 6 hr. shear stressed HUVEC's. Shown in lanes 1,2, and 3 are a 5-fold dilution series of input cDNA amplified in the upper panel with rchd523 primers [(for-atgccgtgtgggtagtc/rev-attttatgggaaggttttaca)] (for-atgccgtgtgggtagtc (SEQ ID NO. 28)/rev-attttatgggaaggttttaca (SEQ ID NO. 29)), and in lanes 4 and 5, a 5-fold dilution series using human actin primers (for-accctgaagtaccccat/rev-tagaagcatttgcggtg). A band at the 1:5 dilution in lane 2 is visible in the 6 hr. sample but not in the control.

FIG.28. DNA (SEQ ID NO. 6) and encoded amino acid (SEQ ID NO. 38) sequence of the rchd523 gene.

FIG.29. Laminar shear stress HUVEC differential display for rchd528. mRNA prepared from control HUVEC (lanes 3,4), 1 hr. (lanes 1,2) or 6 hr. (lanes 5,6) of 10 dyn/cm² laminar shear stress treatment was used in differential display reactions with the forward primer OPI19 (aatgcgggag) (SEQ ID NO. 30) and reverse primer T₁₁XG, which is an equimolar mix of oligonucleotides where X is G,C, or A. The DNA corresponding to marked band, rchd528, was excised and amplified for Northern analysis and subcloning.

Page 17, lines 10 through 13:

FIG.31. Band rchd528 DNA sequence (SEQ ID NO. 7). The sequence was determined by sequencing the insert of pRCHD528, resulting from the ligation of amplified rchd528 sequences into the TA cloning vector.

Page 17, lines 25 through 26:

FIG.35. DNA (SEQ ID NO. 36) and encoded amino acid (SEQ ID NO. 37) sequence of the rchd534 gene.

Page 38, lines 19 through 24:

5.4.1. DIFFERENTIALLY EXPRESSED AND PATHWAY GENE SEQUENCES

The differentially expressed and pathway genes of the invention are listed below, in Table 1. Differentially expressed and pathway gene nucleotide sequences are shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37).

Page 39, line 19 through page 40, line 2:

The genes listed in Table 1 may be obtained using cloning methods well known to those skilled in the art, including but not limited to the use of appropriate probes to detect the genes within an appropriate cDNA or gDNA (genomic DNA) library. (See, for example, Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, which is incorporated by reference herein in its entirety). Probes for the novel sequences reported herein may be obtained directly from the isolated clones deposited with the NRRL, as indicated in Table 2, below. Alternatively, oligonucleotide probes for the

novel genes may be synthesized based on the DNA sequences disclosed herein in FIGs.8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37). Such synthetic oligonucleotides may be similarly produced based on the sequences provided for the previously known genes described in the following references: Cleary et al., 1986, Cell 47: 19-28 (bcl-2); Takahashi et al., 1990, J. Biochem 108: 145-148 (glutathione peroxidase); and Jones et al., 1993, J. Biol. Chem. 268: 9049-9054 (prostaglandin endoperoxide synthase II), each of which is incorporated herein in its entirety.

Page 43, line 33 through Page 44, line 35:

As used herein, "differentially expressed gene" (i.e. target and fingerprint gene) or "pathway gene" refers to (a) a gene containing at least one of the DNA sequences disclosed herein (as shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)), or contained in the clones listed in Table 2, as deposited with the NRRL; (b) any DNA sequence that encodes the amino acid sequence encoded by the DNA sequences disclosed herein (as shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)), contained in the clones, listed in Table 2, as deposited with the NRRL or contained within the coding region of the gene to which the DNA sequences disclosed herein (as shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)) or contained in the clones listed in Table 2, as deposited with the NRRL, belong; (c) any DNA sequence that hybridizes to the complement of the coding

sequences disclosed herein, contained in the clones listed in Table 2, as deposited with the NRRL, or contained within the coding region of the gene to which the DNA sequences disclosed herein (as shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)) or contained in the clones listed in Table 2, as deposited with the NRRL, belong, under highly stringent conditions, e.g., hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65 °C, and washing in 0.1xSSC/0.1% SDS at 68 °C (Ausubel F.M. et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3) and encodes a gene product functionally equivalent to a gene product encoded by sequences contained within the clones listed in Table 2; and/or (d) any DNA sequence that hybridizes to the complement of the coding sequences disclosed herein, (as shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)) contained in the clones listed in Table 2, as deposited with the NRRL or contained within the coding region of the gene to which DNA sequences disclosed herein (as shown in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)) or contained in the clones, listed in Table 2, as deposited with the NRRL, belong, under less stringent conditions, such as moderately stringent conditions, e.g., washing in 0.2xSSC/0.1% SDS at 42 °C (Ausubel et al., 1989, *supra*), yet which still encodes a functionally equivalent gene product.

Page 49, lines 1 through 14:

5.4.2. DIFFERENTIALLY EXPRESSED AND PATHWAY GENE PRODUCTS

Differentially expressed and pathway gene products include those proteins encoded by the differentially expressed and pathway gene sequences described in Section 5.4.1, above. Specifically, differentially expressed and pathway gene products may include differentially expressed and pathway gene polypeptides encoded by the differentially expressed and pathway gene sequences contained in the clones listed in Table 2, above, as deposited with the NRRL, or contained in the coding regions of the genes to which DNA sequences disclosed herein (in FIGS. 8 (SEQ ID NO. 1), 12 (SEQ ID NO. 2), 15 (SEQ ID NO. 3), 18 (SEQ ID NO. 4), 22 (SEQ ID NO. 5), 28 (SEQ ID NO. 38), 31 (SEQ ID NO. 7), and 35 (SEQ ID NOS. 36-37)) or contained in the clones, listed in Table 2, as deposited with the NRRL, belong, for example.

Page 107, line 23, through Page 108, line 2:

First strand cDNA synthesis: For each RNA sample duplicate reactions were carried out in parallel. 400 ng RNA plus DEPC H₂O in a total volume of 10 µl were added to 4 µl T₁₁XX (SEQ ID NO. 31) reverse primer (10 µM) (Operon). The specific primers used in each experiment are provided in the Description of the Figures in Section 4, above. The mixture was incubated at 70°C for 5 min. to denature the RNA and then placed at r.t. 26 µl of reaction mix containing the following components was added to each denatured RNA/primer sample: 8 µl 5x First Strand Buffer (Gibco/BRL, Gaithersburg, MD), 4 µl 0.1M DTT (Gibco/BRL), 2 µl RNase inhibitor (40 units/µl) (Boehringer Mannheim), 4 µl 200 µM dNTP mix, 6 µl H₂O, 2 µl Superscript reverse transcriptase (200 units/µl) (Gibco/BRL). The reactions were mixed gently and incubated for 30 min. at 42°C. 60 µl of

H₂O (final volume = 100 µl) were then added and the samples were denatured for 5 min. at 85 °C and stored at -20 °C.

Page 119, lines 14 through 24:

Lipoproteins were prepared as described, above, in section 6.1.1. Differential display, Northern analysis, RT-PCR, subcloning, and DNA sequencing were carried out as described, above, in Section 6.1.2. For differential display, the primers used were T₁₁CC (reverse) and OPE4 (forward), consisting of 5'GTGACATGCC3' (SEQ ID NO. 33). For RT-PCR, the first strand cDNA was primed with T₁₁CC (SEQ ID NO. 32), and PCR reactions were carried out with rfhma15 primers [(for-catgcctgtagaaaaagggt/rev-cttcatagaatctaagccta)] (for-catgcctgtagaaaaagggt (SEQ ID NO. 34)/rev-cttcatagaatctaagccta) (SEQ ID NO. 35), and mouse γ actin primers (for-cctgatagatgggcactgtgt/rev-gaacacggcattgtcactaact).

Page 124, line 8 through page 125, line 21:

8.2. RESULTS

HUVEC's were activated with 10 units/ml IL-1 β for 1 or 6 hours and compared to resting HUVEC's using differential display. As shown in FIG.5, a band marked rchd005 is present in lanes 11 and 12 (IL-1, 6 hr.) but not in lanes 9 and 10 (control), or lanes 7 and 8 (IL-1, 1 hr.). This band, rchd005, was isolated and subcloned and sequenced. When a probe prepared from this band was used to screen a Northern blot, expression was seen at 6 hr., but not at 1 hr. or in the control (FIG.6). However, when this same probe was hybridized to a Northern blot prepared from shear stressed RNA, according to Paradigm D described in Section 9, below, a different pattern of up-regulation was also seen (FIG.7). Expression was up at 1 hr. and then nearly disappeared by 6 hr. Amplified rchd005 DNA was subcloned and

sequenced. Sequence analysis revealed an approximately 360 bp insert (FIG.8) (SEQ ID NO. 1) with 70% sequence similarity to a cloned shark gene called bumetanide-sensitive Na-K-Cl cotransport protein.

Another IL-1 inducible band, rchd024, is shown in FIG.9. Northern analysis on IL-1 up-regulated RNA reveals a 10 kb message present at 6 hr. (FIG.10) that also shows a low level of up-regulation under shear stress at 6 hr. (FIG.11). The DNA sequence was obtained from subclones of amplified DNA (FIG.12) (SEQ ID NO. 2). Database searching revealed no significant sequence similarities. A PCR amplification experiment determined that the rchd024 gene is located on human chromosome 4.

Band rchd032 was isolated on the basis of its differentially increased expression after 6 hr. treatment with IL-1 (FIG.13), which was confirmed by RT-PCR analysis (FIG.14). Amplified rchd032 sequences were subcloned and sequenced (FIG.15) (SEQ ID NO. 3). No significant homology to any known gene was found.

Band rchd036 was also isolated on the basis of its differential expression 6 hr. after IL-1 treatment (FIG.16). Northern analysis (FIG.17) revealed an 8 kb band which was up-regulated 6 hr. after IL-1 treatment. Another Northern analysis was performed testing rchd036 under the shear stress condition of Paradigm D, which are described in the example in Section 9. below. Interestingly, rchd036 is not induced by shear stress, as indicated by the lack of any band after either 1 hr. or 6 hr. of treatment (FIG.33). This result provides an example of an IL-1-inducible endothelial cell gene that is not regulated by shear stress, indicating that these induction pathways can be separated, and may provide for drugs with greater specificity for the treatment of inflammation and atherosclerosis. The DNA sequence was obtained from subclones of amplified DNA (FIG.18) (SEQ ID NO. 4), and a search of the database revealed no sequence similarities. A PCR amplification experiment determined

that the rchd036 gene is located on human chromosome 15.

Page 128. lines 23 through 27:

Determination of chromosomal location was carried out according to the method described in Section 6.1.3. above. The primers used for rchd523 were (for-atgccgtgtgggtagtc)(SEQ ID NO. 28) and (rev-attttatgggaaggttttaca)(SEQ ID NO. 29) ; and for rchd534 were (for-cttttctgcgtctcccat) and (rev-agacatcagaaactccaacc).

EXHIBIT B
MARKED VERSION OF THE CLAIMS
(Preliminary Amendment Filed February 19, 2002)
U.S. PATENT APPLICATION NO. 09/970,820

Please cancel claims 1-3, 8, and 10-11, without prejudice.

EXHIBIT C
CLEAN VERSION OF PENDING CLAIMS AS AMENDED HEREIN
(Preliminary Amendment Filed February 19, 2002)
U.S. PATENT APPLICATION NO. 09/970,820

67. (New) An antibody which immunospecifically binds to the amino acid sequence of Figure 28.

68. (New) An antibody composition according to claim 67, wherein said antibody is a polyclonal antibody.

69. (New) An antibody composition according to claim 67, wherein said antibody is a monoclonal antibody.

70. (New) An antibody composition according to claim 67, wherein said antibody is a conjugated monoclonal antibody.

71. (New) An antibody composition according to claim 67, wherein said antibody is detectably labeled.

72. (New) An antibody composition according to claim 71, wherein said detectable label is selected from the group consisting of fluorescent labeling compounds, bioluminescent compounds and radioisotopes or any combination thereof.

73. (New) A composition for administration to patients comprising an antibody according to claim 67 together with a physiologically acceptable diluent or carrier.

74. (New) A composition according to claim 73, which is adapted for intravenous administration.

75. (New) A composition according to claim 73, which additionally comprises another therapeutic antibody.

76. (New) An antibody which immunospecifically binds to one or more of the extracellular domains, or portions and/or analogs thereof of the rchd523 amino acid sequence

of Figure 28.

77. (New) An antibody composition according to claim 76, wherein said antibody is a polyclonal antibody.

78. (New) An antibody composition according to claim 76, wherein said antibody is a monoclonal antibody.

79. (New) An antibody composition according to claim 76, wherein said antibody is detectably labeled.

80. (New) An antibody composition according to claim 79, wherein said detectable label is selected from the group consisting of fluorescent labeling compounds, bioluminescent compounds and radioisotopes or any combination thereof.

81. (New) A composition for administration to patients comprising an antibody according to claim 76 together with a physiologically acceptable diluent or carrier.

82. (New) A composition according to claim 81, which is adapted for intravenous administration.

83. (New) A composition according to claim 81, which additionally comprises another therapeutic antibody.

84. (New) An antibody which immunospecifically binds to one or more of the extracellular domains, or portions and/or analogs thereof of the rchd523 amino acid sequence of Figure 28, wherein the extracellular domain analog is an Ig-tailed soluble fusion protein.

85. (New) An antibody composition according to claim 84, wherein said antibody is a polyclonal antibody.

86. (New) An antibody composition according to claim 84, wherein said antibody is a monoclonal antibody.

87. (New) An antibody composition according to claim 84, wherein said antibody

is detectably labeled.

88. (New) An antibody composition according to claim 87, wherein said detectable label is selected from the group consisting of fluorescent labeling compounds, bioluminescent compounds and radioisotopes or any combination thereof.

89. (New) A composition for administration to patients comprising an antibody according to claim 84 together with a physiologically acceptable diluent or carrier.

90. (New) A composition according to claim 89, which is adapted for intravenous administration.

91. (New) A composition according to claim 89, which additionally comprises another therapeutic antibody.

92. (New) An antibody which immunospecifically binds to the gene product encoded by a polynucleotide up-regulated in endothelial cells under increased shear stress, wherein said polynucleotide hybridizes under highly stringent conditions to the complement of (a) the polypeptide coding region from nucleotide residue number 559 to 1683 of SEQ ID NO:6; or (b) the polypeptide coding region of the cDNA contained in plasmid pFCHD523, as deposited with the Agricultural Research Service Culture Collection as Accession Number B-21458, wherein said highly stringent conditions comprise hybridization in 0.5M NaHPO₄, 7% sodium dodecyl sulphate (SDS), 1 mM EDTA at 65C, and washing in 0.1X SSC / 0.1% SDS at 68C.

93. (New) An antibody composition according to claim 92, wherein said antibody is a polyclonal antibody.

94. (New) An antibody composition according to claim 92, wherein said antibody is a monoclonal antibody.

95. (New) An antibody composition according to claim 92, wherein said antibody

is detectably labeled.

96. (New) An antibody composition according to claim 95, wherein said detectable label is selected from the group consisting of fluorescent labeling compounds, bioluminescent compounds and radioisotopes or any combination thereof.

97. (New) A composition for administration to patients comprising an antibody according to claim 92 together with a physiologically acceptable diluent or carrier.

98. (New) A composition according to claim 97, which is adapted for intravenous administration.

99. (New) A composition according to claim 97, which additionally comprises another therapeutic antibody.

100. (New) A method for treating a human patient having a cardiovascular symptom, which comprises administering an antibody according to any one of the claims 67, 76, 84, or 92, wherein said cardiovascular symptom is atherosclerosis, restinosis, or ischemia/reperfusion or any combination thereof, wherein said cardiovascular symptom is ameliorated.

101. (New) A method according to claim 100, wherein the antibody is administered intravenously.

102. (New) A method according to claim 100, wherein the antibody is administered together with another therapeutic antibody.